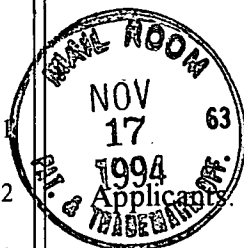


EXHIBIT K

3305



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: A.G. Filler et al.

Attorney Docket No. WRUW16938

Serial No: 08/028,795

Group Art Unit: 3305

Filed: March 8, 1993

Examiner: B. Casler

Title: IMAGE NEUROGRAPHY AND DIFFUSION ANISOTROPY IMAGING

AMENDMENT AND REQUEST FOR RECONSIDERATION

Seattle, Washington 98101

November 14, 1994

11/14/94
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TO THE COMMISSIONER OF PATENTS AND TRADEMARKS:

Please amend the above-identified application as follows and reconsider the claim rejections in the July 11, 1994 Office Action.

AMENDMENT

In the Claims:

Please amend Claims 89, 93, 95, 111, 120, 135, 139, 150, 152, 153, 155, 156, 158 and 159 as follows:

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89. (Amended) A method of utilizing magnetic resonance to determine the shape and position of mammal tissue, said method including the steps of:

(a) exposing an *in vivo* region of a subject to a magnetic polarizing field, the *in vivo* region including non-neural tissue and a nerve, the nerve being a member of the group consisting of peripheral nerves, cranial nerves numbers three through twelve, and autonomic nerves;

(b) exposing the *in vivo* region to an electromagnetic excitation field;

(c) [producing an output indicative of the *in vivo* region's] sensing a resonant response of the *in vivo* region to the polarizing and excitation fields and producing an output indicative of the resonant response;

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1 (d) controlling the performance of the steps (a), (b), and (c) to enhance, in the
2 output produced, the selectivity of said nerve, while the nerve is living in the *in vivo* region of the
3 subject; and

4 (e) processing the output to generate a data set describing the shape and position
5 of said nerve, said data set distinguishing said nerve from non-neural tissue in the *in vivo* region to
6 provide a conspicuity of the nerve that is at least 1.1 times that of the non-neural tissue, without the
7 use of neural contrast agents.

8 ~~93.~~ (Amended) The method of Claim ~~92~~⁷, wherein the step of subtracting further includes
9 the step of determining [the] a registration between the first output and the second output.

10 ~~10~~ ¹⁰ ~~95.~~ (Amended) The method of Claim ~~92~~¹⁰⁵, wherein the non-neural tissue includes fat, and
11 wherein the method includes the step of exposing the *in vivo* region to electromagnetic fields that
12 suppress the contribution of the fat in said first and second outputs prior to the steps exposing the
13 *in vivo* region to said first and second gradients[, the *in vivo* region is exposed to electromagnetic
14 fields that suppress the contribution of the fat in said first and second outputs].

15 ~~111.~~ (Amended) The method of Claim 110, wherein [said steps (a), (b), and (c) to produce
16 a first output in which] the contribution of nerve is enhanced in said output and [as] said steps (a),
17 (b), and (c) are performed a second time to produce a second output in which the contribution of
18 blood vessels is enhanced, [and] wherein said step (e) of processing the output includes the step of
19 processing [the first and] said output and said second output[s] to suppress the blood vessels from
20 said data set.

21 ~~120.~~ (Amended) A method of utilizing magnetic resonance to determine the shape and
22 position of a structure, said method including the steps of:

23 (a) exposing a region to a magnetic polarizing field including a predetermined
24 arrangement of diffusion-weighted gradients, the region including a selected structure that exhibits
25 diffusion anisotropy and other structures that do not exhibit diffusion anisotropy;

1 (b) exposing the region to an electromagnetic excitation field;
2 (c) for each of said diffusion-weighted gradients, [producing an output indicative
3 of the region's] sensing a resonant response of the region to the excitation field and the polarizing
4 field including the diffusion-weighted gradient and producing an output indicative of the resonant
5 response; and

6 (d) vector processing said outputs to generate data representative of anisotropic
7 diffusion exhibited by said selected structure in the region, regardless of the alignment of said
8 diffusion-weighted gradients with respect to the orientation of said selected structure; and

9 (e) processing said data representative of anisotropic diffusion to generate a data
10 set describing the shape and position of said selected structure in the region, said data set
11 distinguishing said selected structure from other structures in the region that do not exhibit diffusion
12 anisotropy.

13 ~~5/60~~ 135. (Amended) A method of utilizing magnetic resonance to determine data
14 representative of diffusion anisotropy exhibited by a structure, said method including the steps of:

15 (a) exposing a region to a suppression sequence of electromagnetic fields that
16 suppresses the electromagnetic responsiveness of structures in the region that do not exhibit diffusion
17 anisotropy, so as to increase the apparent diffusion anisotropy of structures in the region that exhibit
18 diffusion anisotropy, said suppression sequence of electromagnetic fields not including diffusion-
19 weighted magnetic gradients;

20 (b) exposing the region to a predetermined arrangement of diffusion-weighted
21 magnetic gradients, said predetermined arrangement of diffusion-weighted magnetic gradients chosen
22 to:

23 i) emphasize a selected structure in the region exhibiting diffusion
24 anisotropy in a particular direction; and

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1 ii) suppress other structures in the region exhibiting diffusion anisotropy in
2 directions different from said particular direction;

3 (c) for each of said diffusion-weighted gradients, [producing an output indicative
4 of the region's] sensing a resonant response of the region to the diffusion-weighted gradient and
5 producing an output indicative of the resonant response; and

6 (d) processing said outputs to generate data representative of the diffusion
7 anisotropy of the selected structure.

8 139. (Amended) A magnetic resonance apparatus for determining the shape and position of
9 mammal tissue, said apparatus including:

10 (a) [a] polarizing field source means for exposing an *in vivo* region of a subject to
11 a magnetic polarizing field, the *in vivo* region including non-neural tissue and a nerve, the nerve being
12 a member of the group consisting of peripheral nerves, cranial nerves numbers three through twelve,
13 and autonomic nerves;

14 (b) [an] excitation and output arrangement means positioned near said polarizing
15 field source means for exposing the subject to an electromagnetic excitation field;

16 (c) [a] sequence controller means coupled to said polarizing field source means
17 and said excitation and output arrangement means for controlling the operation of said polarizing field
18 source means and said excitation and output arrangement means so that the polarizing field and the
19 excitation field cooperatively induce a resonant response in the *in vivo* region to enhance the
20 selectivity of said nerve while the nerve is *in vivo* and living, said excitation and output arrangement
21 means further for sensing the resonant response of the *in vivo* region and producing an output
22 indicative of the resonant response of the *in vivo* region at a time determined by said sequence
23 controller means; and

24 (d) [a] processor means for processing said output to produce a data set describing
25 the shape and position of said nerve, said data set distinguishing the nerve from non-neural tissue in

1 the *in vivo* region to provide a conspicuity of the nerve that is at least 1.1 times that of the non-neural
2 tissue, without requiring the use of neural contrast agents.

3 140. (Amended) The apparatus of Claim 139, wherein said excitation and output
4 arrangement means includes a phased-array coil system.

5 150. (Amended) A magnetic resonance apparatus for determining the shape and position of
6 a structure, said apparatus including:

7 (a) [a] polarizing field source means for exposing a region to a magnetic polarizing
8 field including a predetermined arrangement of diffusion-weighted gradients, the region including a
9 selected structure that exhibits diffusion anisotropy and other structures that do not exhibit diffusion
10 anisotropy;

11 (b) [an] excitation and output arrangement means positioned near said polarizing
12 field source means for:

13 i) exposing the region to an electromagnetic excitation field; and
14 ii) [producing,] for each of said diffusion-weighted gradients, [an output
15 indicative of the region's] sensing a resonant response of the region to the excitation field and the
16 polarizing field including the diffusion-weighted gradient and producing an output indicative of the
17 resonant response; and

18 (c) [a] processor means coupled to said excitation and output arrangement means
19 for:

20 i) vector processing said outputs to generate data representative of
21 anisotropic diffusion exhibited by the selected structure in the region, regardless of the alignment of
22 said diffusion-weighted gradients with respect to the orientation of said selected structure; and

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ii) processing said data representative of anisotropic diffusion to generate a data set describing the shape and position of said selected structure in the region, said data set distinguishing said selected structure from other structures in the region that do not exhibit diffusion anisotropy.

57 152. (Amended) The apparatus of Claim 151, wherein :

said processor means is further for analyzing said data representative of anisotropic diffusion to determine an effective direction of the anisotropic diffusion exhibited by said neural tissue, so as to determine an optimal orientation for diffusion-weighted gradients;

said polarizing field source means is further for exposing the region to two additional diffusion-weighted gradients respectively substantially parallel to and substantially perpendicular to said effective direction;

said excitation and output arrangement means is further for producing two additional outputs indicative of the region's resonant responses respectively to said two additional diffusion-weighted gradients; and

said processor means is further for determining the difference between said two additional outputs to generate said data set describing the shape and position of said neural tissue.

58 153. (Amended) The apparatus of Claim 151, wherein said data set describing the shape and position of said neural tissue describes the shape and position of a selected cross section of said neural tissue, and said apparatus is further for generating additional data sets describing different cross sections of said neural tissue, and said processor means is further for calculating a further data set that describes the three dimensional shape and position of a segment of said neural tissue by:

analyzing the data representative of anisotropic diffusion to determine how to relate said data set and said additional data sets describing the shape and position of cross sections of said neural tissue; and

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1 based upon the results of said analyzing the data representative of anisotropic diffusion,
2 combining said data set and said additional data sets to generate said further data set that describes
3 the three dimensional shape and position of the segment of said neural tissue, thereby allowing a three
4 dimensional shape and position of curved neural tissue to be described.

5 ~~60~~ ~~155~~ (Amended) The apparatus of Claim ~~150~~ ⁵⁵, wherein:

6 said processor means is further for analyzing said data representative of anisotropic diffusion
7 to determine an effective direction of the anisotropic diffusion exhibited by said selected structure, so
8 as to determine an optimal orientation for diffusion-weighted gradients;

9 said polarizing field source means is further for exposing the region to two additional
10 diffusion-weighted gradients respectively substantially parallel to and substantially perpendicular to
11 said effective direction;

12 said excitation and output arrangement means is further for producing two additional outputs
13 indicative of the region's resonant responses respectively to said two additional diffusion-weighted
14 gradients; and

15 said processor means is further for determining a difference between said two additional
16 outputs to generate said data set describing the shape and position of said selected structure.

17 ~~61~~ ~~156~~ (Amended) The apparatus of Claim ~~150~~ ⁵⁵, wherein said data set describing the shape
18 and position of said selected structure describes the shape and position of a selected cross section of
19 said selected structure, and said apparatus is further for generating additional data sets describing
20 different cross sections of said selected structure, and said processor means is further for determining
21 a further data set that describes the three dimensional shape and position of a segment of said selected
22 structure by:

23 analyzing the data representative of anisotropic diffusion to determine how to relate said data
24 set and said additional data sets describing the shape and position of cross sections of said selected
25 structure; and

1 based upon the results of said analyzing the data representative of anisotropic diffusion,
2 combining said data set and said additional data sets to generate said further data set that describes
3 the three dimensional shape and position of the segment of said selected structure, thereby enabling a
4 three dimensional shape and position of curved structure exhibiting anisotropic diffusion to be
5 described.

6 ~~54~~ 158. (Amended) A magnetic resonance apparatus for determining data representative of
7 the diffusion anisotropy exhibited by a structure, said apparatus including:

8 (a) [an] excitation and output arrangement means for exposing a region to a
9 suppression sequence of electromagnetic fields that suppresses the electromagnetic responsiveness of
10 structures in the region that do not exhibit diffusion anisotropy, so as to increase the apparent
11 diffusion anisotropy of structures in the region that exhibit diffusion anisotropy, said suppression
12 sequence of electromagnetic fields not including diffusion-weighted magnetic gradients;

13 (b) [a] polarizing field source means positioned near said excitation and output
14 arrangement means for exposing the region to a predetermined arrangement of diffusion-weighted
15 magnetic gradients chosen to:

16 i) emphasize a selected structure in the region exhibiting diffusion
17 anisotropy in a particular direction; and

18 ii) suppress other structures in the region exhibiting diffusion anisotropy in
19 directions different from said particular direction, said excitation and output arrangement means
20 further for [producing, for each of said diffusion-weighted gradients, an output indicative of the
21 region's] sensing a resonant response of the region to the diffusion-weighted gradient and producing
22 an output indicative of the resonant response, for each of said diffusion-weighted gradients; and

23 (c) [a] processor means coupled to said excitation and output arrangement means
24 for processing said outputs to generate data representative of the diffusion anisotropy of the selected
25 structure.

159. (Amended) The apparatus of Claim 158, wherein said processor means is further for processing said data representative of the diffusion anisotropy of the selected structure to produce a data set that describes the shape and position of the selected structure.

REMARKS

In the July 11, 1994 Office Action, the Examiner rejected Claims 89, 120, 135, 93, 95, 111, 139, 150, 158, 151-157, 159-161 and claims depending thereon as being indefinite. Except for Claims 93, 127, 129 and 132, the pending claims of this application (Claims 89-161) were rejected as being either anticipated or obvious in view of various prior art references. The Examiner indicated that Claims 93, 127, 129 and 132 would be allowable if rewritten in independent form and modified to overcome the indefiniteness rejections. Applicants respectfully request that the claim rejections be reconsidered.

Section 112 Rejections

Claims 89, 120, 135, 93, 95, 111, 139, 150 and 158 have been amended to overcome the rejection of these claims as being indefinite. For example, Claims 89, 120 and 135 have been amended to specify a step of sensing a resonant response. Similarly, with respect to the Examiner's objection to Claims 139, 150 and 158 as failing to recite a structure to affect the detection of the resonant response, the claims have been amended to indicate that the "excitation and output arrangement means" performs this function, i.e., senses the resonant response.

With respect to Claims 151-157 and 159-161, remarks accompanying the rejection of these claims state that the claims "do not set forth any structure to further limit the apparatus and recite only functional language." The applicants respectfully disagree. For example, independent Claim 150 specifies a magnetic resonance apparatus including various means constructed for distinguishing a selected structure that exhibits diffusion anisotropy from other surrounding structures that do not exhibit diffusion anisotropy. Claim 151 depends upon Claim 150 and further specifies that the selected structure is neural tissue in a mammal and the other structures are non-neural tissue in the

1 mammal. As such, dependent Claim 151 specifies that the various means recited in Claim 151 are
2 constructed to distinguish neural tissue in a mammal, thereby further limiting the claim. Thus, the
3 "functional language" in Claim 151 further limits Claim 150. The applicants would like to also call
4 the Examiner's attention to M.P.E.P. § 608.01(n), p.600-39, column 2, paragraph 2, which states:

5 A dependent claim does not lack compliance with 35 U.S.C. § 112, fourth paragraph,
6 simply because there is a question as to (1) the significance of the further limitation
7 added by the dependent claim, or (2) whether the further limitation in fact changes the
8 scope of the dependent claim from that of the claim from which it depends. The test
9 for a proper dependent claim under the fourth paragraph of 35 U.S.C. § 112 is
10 whether the dependent claim includes every limitation of the claim from which it
11 depends. The test is not one of whether the claim differs in scope.

12 Thus, while 35 U.S.C. § 112 requires that a dependent claim shall "specify a further limitation of the
13 subject matter claimed," the significance of the further limitation added by the dependent claim should
14 not be questioned. Accordingly, applicants respectfully submit that the rejection of Claims 151-157
15 and 159-161 under 35 U.S.C. § 112 should be withdrawn.

16 Prior Art Rejections

17 Novelty Rejections

18 Independent Claims

19 Rejections over Hajnal et al.

20 Method Claims 89-91, 96-106, 108, 120, 121, 123-126, 128, and 135-138 were rejected as
21 being anticipated by Hajnal et al. Remarks accompanying these rejections state that Hajnal et al.
22 teaches MR imaging of a structure within the nervous system that exhibits diffusion anisotropy by the
23 use of polarizing and excitation fields, diffusion-weighted gradients, and analyzing fascicles found in
24 peripheral nerves. The rejected claims include independent Claims 89, 120, and 135.

25 Independent Claim 89 specifies a method of utilizing magnetic resonance to generate a data
set that describes the position and shape of a *peripheral nerve, one of the cranial nerves nos. 3-12 or
an autonomic nerve*. The claim specifies that the data set distinguishes the nerve from non-neural

1 tissue to provide a conspicuity of the nerve that is at least 1.1 times that of the non-neural tissue. The
2 nerve "conspicuity" refers to the contrast (in, for example, the intensity or color) between the nerve
3 and the image background. *See*, page 16, lines 4-7. That is, the conspicuity of a particular tissue
4 refers to the visual contrast between that tissue and surrounding background tissue. The methods
5 taught by Hajnal et al. and the other prior art references of record do not teach a method that meets
6 these functional limitations of Claim 89. The prior art methods cannot provide the specified level of
7 conspicuity for a peripheral nerve, one of the cranial nerves 3-12, or an autonomic nerve. Rather, the
8 prior art methods can only provide the specified level of neural-tissue conspicuity for the brain, the
9 spinal cord, or the optic nerve.

10 In particular, Hajnal et al. discloses a method of using diffusion-weighted gradients that can
11 distinguish neural tissue in the brain at a conspicuity that is at least 1.1 times that of the non-neural
12 tissue. *See, e.g.*, Hajnal et al., Figure 5. However, the method taught by Hajnal et al. is not able to
13 achieve such conspicuity for a peripheral nerve, one of the cranial nerves 3-12, or an autonomic
14 nerve. Hajnal et al. does disclose that cranial and peripheral nerves demonstrate anisotropy
15 properties, *e.g.*, on page 14, the bottom of column 1. However, the diffusion-weighted gradient
16 method taught by Hajnal et al. is not able to provide the required level of conspicuity for the nerves
17 specified in Claim 89. For example, Figure 20 of Hajnal et al. illustrates the results of using the
18 disclosed method to attempt to image the sciatic nerve of a human. While the sciatic nerve can be
19 vaguely identified when pointed out by an arrow, the sciatic nerve is clearly not shown with a
20 conspicuity that is at least 1.1 times that of non-neural tissue in the image.

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1 Instead, fat and bone tissue have the highest conspicuity, i.e., the fat and bone tissue appear
2 very bright with respect to surrounding background tissue.¹ In Figure 20b of Hajnal et al., the fat
3 appears much brighter than both the adjacent sciatic nerve and the surrounding muscle fat so that the
4 fat has a very high conspicuity. In contrast, the sciatic nerve can barely be distinguished from the
5 surrounding muscle tissue. Therefore, it is clear that the conspicuity of the sciatic nerve is not greater
6 than that of the surrounding fat. Accordingly, the requirement in Claim 89 that the method achieves a
7 conspicuity for the nerve tissue that is at least 1.1 times that of non-neural tissue (e.g., fat) is clearly
8 not met by the method taught by Hajnal et al.

9 The present inventors were the first to provide and demonstrate a method of utilizing
10 magnetic resonance to describe the shape and position of a peripheral nerve, one of the cranial
11 nerves 3-12 or an autonomic nerve with a conspicuity of the nerve that is at least 1.1 times that of
12 non-neural tissue, without the use of a neural contrast agent. For example, Figures 20 and 21 of the
13 present patent application show images of the thigh area of a human, analogous to Figure 20 in Hajnal
14 et al. However, unlike Figure 20 in Hajnal et al., the sciatic nerve shown in Figures 20 and 21 of the
15 present application is highly conspicuous, i.e., the contrast between the sciatic nerve and the
16 surrounding background tissue is high.² Because the prior art does not disclose a method of imaging
17 a peripheral nerve, one of the cranial nerves 3-12, or an autonomic nerve with a conspicuity at least
18 1.1 times that of non-neural tissue, Claim 89 specifies a novel and non-obvious method over Hajnal et
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21 ¹As seen in Figure 20b of Hajnal et al., the sciatic nerve is surrounded to the left by fat and to the right by
22 muscle. It is true that there is a significant contrast between the sciatic nerve and the fat because the intensity of the fat
23 is much higher than that of the sciatic nerve. However, the muscle tissue to the right of the sciatic nerve has an
24 intensity very close to that of the sciatic nerve, so that there is virtually no conspicuity between the sciatic nerve and
25 muscle tissue. Thus, while Figure 20b is described as showing the sciatic nerve somewhat enhanced, in fact, the sciatic
nerve can barely be distinguished from the surrounding muscle tissue.

26 ²Specifically, the sciatic nerve is seen approximately in the center of Figure 20, and Figure 21 is a
magnification of Figure 20 showing the sciatic nerve enlarged. The sciatic nerve is brighter than all immediately
surrounding tissue. In fact, the image of the sciatic nerve is so clear that the fascicular structure of the nerve can be
seen, and unlike Figure 20 of Hajnal et al., the fat surrounding the sciatic nerve is suppressed.

1 al. and the other prior art. In addition to the prior art not meeting these function limitations, the prior
2 art does not teach the particular process step specified in the claims depending upon Claim 89, as
3 discussed in detail below.

4 With respect to the rejection of independent Claim 120 as being anticipated by Hajnal et al.,
5 applicants respectfully submit that Hajnal et al. does not teach or suggest the claimed method.
6 Independent Claim 120 specifies a method of determining the shape and position of a selected
7 structure exhibiting diffusion anisotropy by utilizing diffusion-weighted gradients *and vector*
8 *processing the corresponding outputs*, so that the shape and position of the selected diffusion
9 anisotropic structure can be determined *regardless of the alignment of the diffusion-weighted*
10 *gradients with respect to the orientation of the structure*.

11 Hajnal et al. does not teach this use of diffusion-weighted gradients in combination with
12 vector processing. Rather, Hajnal et al. teaches that the diffusion-weighted gradients must run either
13 perpendicular or parallel to the fibers of the neural tissue (i.e., the anisotropic structure) being
14 imaged. In particular, on page 8 Hajnal et al. specifies that:

15 To highlight a particular tract using [anisotropically restricted diffusion] ARD imaging,
16 it is necessary that sufficient fibers run perpendicular to the gradient being used.

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18 The same general considerations apply to relative loss of signal from tracts or fibre
19 pathways using sensitizing gradients parallel to their predominant direction. When the
20 correct orientation is used, the loss of signal intensity can be dramatic.

21 Thus, in the prior art methods using diffusion-weighted imaging, such as that disclosed in Hajnal et
22 al., the direction of the fibers to be imaged must be known in order for the methods to be effective.
23 Unfortunately, many times the direction of diffusion exhibited by a structure is not known, so that
24 some form of preliminary analysis must first be performed to determine the direction of diffusion. For
25 example, as disclosed in the present patent application, the direction of the diffusion-weighted
gradient can be varied until the maximum image intensity for a selected diffusion anisotropic structure

1 is found. However, such preliminary steps can significantly increase the processing time required to
2 generate an image.

3 The present invention overcomes this problem by using a selected arrangement of
4 diffusion-weighted gradients in combination with vector processing, so that the shape and position of
5 a selected structure exhibiting diffusion anisotropy can be effectively determined--regardless of the
6 alignment of the gradients with respect to the orientation of the selected structure (as described in the
7 present application on pages 26-30). As specifically specified by Claim 120, the method includes the
8 steps of: (a) exposing a region to a predetermined arrangement of magnetic diffusion-weighted
9 gradients; (b) exposing the region to an electromagnetic excitation field; (c) sensing and producing
10 outputs indicative of the region's resonant response to each of the diffusion-weighted gradients;
11 (d) *vector processing the outputs to generate data representative of anisotropic diffusion exhibited*
12 *by a selected structure in the region*, regardless of the alignment of diffusion-weighted gradients with
13 respect to the orientation of the selected structure; and (e) processing the data representative of
14 anisotropic diffusion to generate a description of the shape and position of the selected structure, so
15 as to distinguish the selected structure from other structures in the region that do not exhibit diffusion
16 anisotropy. Since the prior art including Hajnal et al. does not teach or suggest vector processing
17 outputs generated in response to diffusion-weighted gradients, independent Claim 120 is novel and
18 non-obvious.

19 Similarly, with respect to the rejection of independent Claim 135 as being anticipated by
20 Hajnal et al., applicants respectfully submit that the claim is patentable over Hajnal et al. and the other
21 prior art of record. Claim 135 specifies a method of determining the diffusion anisotropy exhibited by
22 a selected structure in a region that includes other structures that do not exhibit diffusion anisotropy.
23 As specified by Claim 135, the method includes the steps of: (a) *exposing the region to a suppression*
24 *sequence of electromagnetic fields that suppresses the electromagnetic responsiveness of structures*
25 *in the region that do not exhibit diffusion anisotropy, the suppression sequence of electromagnetic*

1 *fields not including diffusion-weighted magnetic gradients*; (b) exposing the region to a
2 predetermined arrangement of diffusion-weighted magnetic gradients (c) sensing the resonant
3 response of the region to the diffusion-weighted gradients and producing corresponding outputs; and
4 (d) processing the outputs to generate data describing the diffusion anisotropy of the selected
5 structure.

6 The invention specified by Claim 135 is based upon the inventors' discovery of the benefits of
7 utilizing a suppression sequence of electromagnetic fields in addition to and prior to the use of
8 diffusion-weighted magnetic gradients. In particular, the inventors discovered that not only does the
9 use of a suppression sequence in combination with diffusion-weighted imaging (i.e., diffusion-
10 weighted magnetic gradients) eliminate undesirable non-anisotropic tissue, the prior use of a
11 suppression sequence actually increases the responsiveness of anisotropic tissue to subsequent
12 diffusion-weighted magnetic gradients. Hajnal et al. in no way teaches or suggests this discovery.

13 Hajnal et al. only teaches the use of diffusion-weighted magnetic gradients. As stated in
14 Hajnal et al. on page 2, column 1, lines 4-9,

15 By deliberately applying large magnetic field gradients in particular directions,
16 diffusion can be made the dominant image contrast mechanism, enabling variations in
diffusion to be visualized, including their directional dependence.

17 And, as stated on page 10, column 2, lines 11-13:

18 Oblique sensitization was implemented by simultaneously applying two or more
19 gradient pulses in the X-, Y-, or Z- directions.

20 Hajnal et al. does not use or suggest the use of a suppression sequence prior to the diffusion-weighted
21 magnetic gradients.

22 Rejections over Suzuki et al.

23 With respect to the apparatus claims, Claims 139, 144-161 were rejected as being anticipated
24 by Suzuki et al. Of these rejected claims, Claims 139, 150 and 158 are independent claims. In
25 addition to specifying polarizing field source means, excitation and output arrangement means, and

1 processor means, independent Claims 139, 150 and 158 specify functional limitations for each of
2 these elements. The Examiner apparently did not consider these functional limitations because he
3 stated "the functional recitations lack proper means phraseology." These claims have been amended
4 to use "means" phraseology, and as such, the functional limitations should be considered. The
5 functional limitations in independent apparatus Claims 139, 150, and 158 respectively correspond to
6 the functional limitations in independent method Claims 89, 120 and 135, which as explained above
7 present patentable subject matter. Accordingly, the applicants respectfully submit that independent
8 apparatus Claims 139, 150 and 158 are patentable over Suzuki et al. and the other prior art of record.

9 Suzuki et al. teaches an imaging system that includes a surface coil for imaging the brain's
10 surface anatomy. See, column 4, line 42-45. The system uses a longer-than-normal echo time to
11 suppress fat on the surface of the brain. Column 4, lines 45-49. The system includes coils 2 for
12 generating gradient magnetic fields *to position imaging information* to a predetermined portion of the
13 brain, as is commonly done in magnetic resonance imaging. See, column 3, lines 20-23. These
14 teachings of Suzuki et al. do not teach or suggest the functional limitations specified in Claims 139,
15 150 and 158.

16 Similar to previously described method Claim 89, corresponding apparatus Claim 139 defuses
17 controller means that controls the operation of the polarizing field source means and the excitation
18 and output arrangement means to enhance the selectivity of a peripheral nerve, cranial nerves 3-12, or
19 an autonomic nerve. The processor means processes outputs generated by the excitation and output
20 arrangement means to produce a data set that distinguishes the nerve from non-neural tissue to
21 provide a conspicuity of the nerve that is at least 1.1 times that of the non-neural tissue. The
22 Suzuki et al. reference does not disclose or suggest such an arrangement -- Suzuki et al. merely
23 images the surface of the brain, which is much larger than peripheral nerves, cranial nerves 3-12 and
24 autonomic nerves. Thus, Suzuki et al. does not teach "apparatus means" that meet the limitations in
25 Claim 139, or, as outlined below, in the claims depending on Claim 139.

1 Similar to previously described method Claim 120, corresponding apparatus Claim 150
2 specifies determining the shape and position of a selected structure exhibiting diffusion anisotropy by
3 utilizing diffusion-weighted gradients and vector processing the resulting outputs, so that the shape
4 and position of the selected diffusion anisotropic structure can be determined regardless of the
5 alignment of the diffusion-weighted gradients. Suzuki et al. teaches neither the use of diffusion-
6 weighted gradients (i.e., diffusion-weighted imaging) nor vector processing of the resulting outputs.
7 Although Suzuki et al. does describe the use of gradient magnetic fields to provide locational (i.e.,
8 position) information, such fields do not correspond to diffusion-weighted gradients which are used
9 to enhance structures exhibiting diffusion anisotropy.

10 As with respect to previously described method Claim 135, corresponding apparatus
11 Claim 158 specifies the use of a suppression sequence of electromagnetic fields followed by diffusion-
12 weighted gradients. In particular, the excitation and output arrangement means generate a
13 suppression sequence of electromagnetic fields that suppresses the electromagnetic responsiveness of
14 non-anisotropic structures, and the polarizing field source means generate a pre-determined
15 arrangement of diffusion-weighted gradients. Not only does Suzuki et al. not teach the use of
16 diffusion-weighted gradients, it in no way suggests pretreating a region with a suppression sequence
17 of electromagnetic fields prior to the use of diffusion-weighted gradients.

18 Dependent Claims

19 As each of the independent claims are patentable over the prior art, applicants respectfully
20 submit that each of the dependent claims rejected as being anticipated by either Hajnal et al. or
21 Suzuki et al. are also patentably distinct. Furthermore, the rejected dependent claims specify
22 additional limitations that further patentably distinguish the claims.

23 Claims 90, 91, 96-106 and 108, which each depend upon independent Claim 89, were rejected
24 as being anticipated by Hajnal et al. The following discusses some of the further patentable
25 limitations specified by these claims.

1 Claims 99 and 101 specify that the output produced by sensing the region's resonant response
2 is analyzed for fascicles, which are found in peripheral nerves, cranial nerves 3-12, and autonomic
3 nerves. Nowhere in Hajnal et al. or the other prior art of record is there a suggestion that the image
4 data be examined for fascicular structure. This fact is not surprising because neither Hajnal et al. nor
5 the other prior art of record teach a method that provides a sufficiently conspicuous image of nerve
6 tissue to make identification of nerve fascicles possible. Claims 100 and 102, which respectively
7 depend upon Claims 99 and 101, specify that the identification of fascicular structures is used to
8 suppress signals from tissue that is not fascicular. By performing this additional processing, all
9 structures other than nerves can be suppressed. This further aspect of the invention is also not
10 suggested by Hajnal et al. or the other prior art of record.

11 Claim 103, which depends directly upon Claim 89, specifies that the characteristic spin-spin
12 relaxation coefficient T_2 of peripheral nerves, cranial nerves 3-12, and autonomic nerves is exploited
13 to better determine the shape and position of the nerve tissue. The inventors of the present
14 application discovered that nerves exhibit a relatively long spin-spin relaxation coefficient T_2 . In the
15 past it was believed that the spin-spin relaxation coefficient T_2 of nerves is relatively short.³ Because
16 the inventors of the present invention discovered that nerve tissue actually has a relatively long spin-
17 spin relaxation time T_2 , they were able to develop an imaging method that exploits this characteristic
18 of nerves to enhance the selectivity with which nerves are made evident, as specified by Claim 103.
19 Accordingly, Claim 103 is patentably distinct from Hajnal et al. and the other prior art of record.
20 Claim 104, which depends upon Claim 103, specifies one way of exploiting the relatively long spin-
21 spin relaxation time T_2 of nerves, i.e., by use of an echo time that is greater than 60 milliseconds.
22
23

24 ³For example, in M.E. Moseley et al., "Anisotropy in Diffusion-Weighted MRI," *Magnetic Resonance in*
25 *Medicine*, 19:321 (1991), on page 325, in the caption accompanying Figure 3, second sentence, the authors state that a
nerve has a relatively short T_2 relaxation time. (A copy of this document was previously included in an information
disclosure statement as item O10.)

1 Claim 105, which depends upon Claim 104, specifies that this approach results in a suppression of
2 muscle tissue, which was previously incorrectly believed to have a longer spin-spin relaxation time
3 than nerves. Claim 106, which depends upon Claim 105, specifies that fat suppression is used in
4 combination with the long echo time. Each of these dependent claims involve further patentably
5 distinct limitations.

6 Claim 108, which depends directly upon Claim 89, specifies that the excitation fields are
7 applied so as to induce a magnetization transfer from non-anisotropically diffusing water in the region
8 to anisotropically diffusing water in the nerve, so that the nerve is more readily distinguished from
9 non-neural tissue. Nowhere in Hajnal et al. or the other prior art of record is there a suggestion of
10 inducing a magnetization transfer of energy in this manner to increase the selectivity of nerves. As
11 explained in the present application at page 38, line 33, through page 39, line 10, this aspect of the
12 invention is based upon the fact that there is an efficient exchange from non-anisotropically diffusing
13 water to anisotropically diffusing water in nerves. In contrast, muscle surrounding nerves do not
14 exhibit this efficient exchange of magnetization. Thus, by exploiting the differential sensitivity
15 between nerve and muscle to magnetization transfer, the selectivity of nerves is further improved.

16 Claim 97, which depends upon Claim 89, specifies that the method includes exciting fat in a
17 manner designed to suppress the contribution of the fat, so as to better distinguish nerves from fat.
18 As previously explained with respect to independent Claim 135, Hajnal et al. merely describes the use
19 of diffusion-weighted imaging; it does not teach or suggest exciting fat so as to suppress the
20 contribution of fat.

21 Claim 96, which depends upon Claims 91 and 89, specifies that a predetermined arrangement
22 of diffusion-weighted gradients are used to produce a separate output associated with each gradient.
23 The claim further specifies that the separate outputs are vector processed to generate data describing
24 the shape and position of the nerve. As previously explained with respect to independent Claim 120,
25 Hajnal et al. does not teach the use of vector processing separate outputs so as to determine the shape

1 and position of a nerve. Rather, because Hajnal et al. does not recognize the possibility of using
2 vector processing, Hajnal et al. teaches that the diffusion-weighted gradients must run either
3 perpendicular or parallel to the fibers of the neural tissue being imaged. A perpendicular or parallel
4 orientation is not required when vector processing, as provided by the present invention, is used.

5 Claims 121, 123-126 and 128, which each depend upon Claim 120, were also rejected as
6 being anticipated by Hajnal et al. The following outlines some of the further patentable distinctions
7 that these dependent claims specify beyond the limitations in independent Claim 120.

8 Claim 123 specifies that the data (generated by vector processing) that describe the
9 anisotropic diffusion of curved neural tissue is used to generate a description of the three-dimensional
10 shape and position of the curved neural tissue. In this method, the data representative of the
11 anisotropic diffusion is used to determine how to combine data describing different cross sections of
12 the curved neural tissue. Dependent Claim 124, which depends upon Claim 123, further specifies that
13 the effective direction of the anisotropic diffusion is used when determining how to combine the data
14 describing the various cross sections of the neural tissue. Claim 125 specifies that an effective vector
15 representative of the anisotropic diffusion exhibited by the neural tissue is determined by analyzing
16 resonant responses after three orthogonal diffusion-weighted gradients are applied. Claim 126, which
17 depends upon Claim 125, further specifies that the shape and position of the neural tissue are based
18 upon the length of the effective vector that describes the anisotropic diffusion. Alternatively, as
19 specified by Claim 128, which depends upon Claim 125, the shape and position of the neural tissue
20 can be based upon an angle defining in part, the direction of the effective vector that describes the
21 anisotropic diffusion.

22 Not only does Hajnal et al. not teach or suggest the use of vector processing as specified in
23 independent Claim 120, Hajnal et al. and the other prior art of record do not teach these further
24 aspects of the claims dependent upon Claim 120.

25 ///

1 Apparatus Claims 151-157, which depend upon independent Claim 150, were rejected as
2 being anticipated by Suzuki et al. As previously explained with respect to Claim 150, Suzuki et al.
3 does not teach or suggest an apparatus that vector processes outputs generated in response to
4 diffusion-weighted gradients to generate a data set describing the shape and position of a diffusion
5 anisotropic structure, regardless of the alignment of the diffusion-weighted gradients. Suzuki et al.
6 also does not teach or suggest the further limitations specified in dependent Claims 151-157. The
7 further limitations specified by these dependent claims were apparently not considered based on the
8 view that the claims did not contain proper "means" phraseology. The claims have been amended to
9 use conventional "means" phraseology, so that the further patentably distinct limitations specified in
10 the dependent claims should now be considered.

11 For example, dependent Claim 152 specifies that: the "processor means" determines an
12 effective direction of the anisotropic diffusion exhibited by the neural tissue; the "polarizing field
13 source means" exposes the neural tissue to two additional diffusion-weighted gradients oriented
14 substantially parallel to and substantially perpendicular to the anisotropic-diffusion effective direction;
15 the "excitation and output arrangement means" produces two additional outputs; and the "processor
16 means" determines the difference between the two additional outputs to determine the shape and
17 position of the neural tissue. Dependent Claim 155 is similar to Claim 152, except that Claim 152
18 depends upon Claim 150 through Claim 151, whereas Claim 155 depends directly upon Claim 150.
19 These further limitations correspond to dependent method Claim 132, which the Examiner said
20 contained patentable subject matter.

21 Dependent Claim 153 specifies that the "processor means" is further for calculating a data set
22 describing the three-dimensional shape and position of a segment of neural tissue by: generating data
23 sets describing selected cross sections of neural tissue; analyzing generated data that are
24 representative of the anisotropic diffusion of the neural tissue; and based upon the results of the
25 analysis, combining the data sets of the cross sections -- as described with respect to corresponding

1 method Claim 123. Dependent Claim 156 is similar to dependent Claim 153, except that Claim 156
2 depends directly upon Claim 150, whereas Claim 153 depends upon Claim 150 through Claim 151.

3 These further limitations in Claims 152, 153 and 156 are in no way suggested by Suzuki et al.

4 Obviousness Rejections

5 Rejections over Hajnal et al., Suzuki et al., and Bydder et al.

6 Claims 107, 109, 110-114, 116-119, 130, 131, 133 and 134 were rejected as being obvious
7 over the combination of Hajnal et al., Suzuki et al., and Bydder et al. Remarks accompanying these
8 rejections state that Hajnal et al. teaches MR imaging of a neural structure that exhibits diffusion
9 anisotropy by the use of polarizing and excitation fields, including diffusion-weighted gradients. The
10 remarks further state that Hajnal et al. does not teach suppressing fat or the use of a splint to
11 immobilize a patient, but that Suzuki et al. teaches suppressing fat on the surface of a brain and
12 Bydder et al. teaches patient immobilization, and that it would be obvious to combine these teachings.
13 Applicants respectfully disagree.

14 Claims 107, 109, 110-114, and 116-119 each depend upon Claim 89, either directly or
15 through other dependent claims. As previously explained, Hajnal et al. does not teach the functional
16 limitations specified in Claim 89, i.e., generating an image of a peripheral nerve, one of the cranial
17 nerves 3-12 or an autonomic nerve, so as to distinguish the nerve from non-neural tissue to provide a
18 conspicuity of the nerve that is at least 1.1 times that of the non-neural tissue. The same is true for
19 both Suzuki et al. and Bydder et al. Suzuki et al. teaches a system for imaging the surface of a brain;
20 the system is not effective for imaging peripheral nerves, cranial nerves 3-12 or autonomic nerves.
21 Similarly, Bydder et al. is limited to imaging tumors in the brain.

22 The dependent claims specify further limitations not shown or suggested by the prior art.
23 Claim 110, which depends upon Claim 89, specifies that the magnetic and electromagnetic fields are
24 controlled to suppress the contribution of blood vessels in the region from the produced outputs.
25 Claim 111, which depends upon Claim 110, further specifies that blood vessels are suppressed by

1 producing a first output in which the contribution of nerve is enhanced, producing a second output in
2 which the contribution of blood vessels is enhanced, and processing the two outputs to suppress the
3 blood vessels. Claim 112, which depends upon Claim 89, specifies that the method suppresses both
4 blood vessels and cerebral spinal fluid.

5 Hajnal et al., Suzuki et al., and Bydder et al. clearly do not teach suppressing blood vessels
6 and/or cerebral spinal fluid as specified by Claims 110-112. In addition, there is no suggestion in
7 these references that would suggest their combination.

8 Claim 116, which depends upon Claim 89, specifies that a read-out gradient rephasing pulse
9 and a slice-selective excitation pulse are used, and that the read-out gradient rephasing pulse is
10 positioned just before the resonant response is produced. This pulse arrangement is in sharp contrast
11 to prior art systems in which the read-out gradient rephasing pulse is positioned directly after the
12 generation of the slice-selective excitation pulse. As a result of this new technique, undesirable cross-
13 terms are reduced. Claim 117, which depends upon Claim 116, further specifies that a two-part phase
14 encoding gradient is used—as opposed to the one-part phase encoding gradient used in the prior art.
15 This step further reduces the appearance of undesirable cross-terms.

16 These aspects of the invention are in no way taught or suggested by the prior art including
17 Hajnal et al., Suzuki et al., and Bydder et al.

18 Claims 130, 131, 133, and 134 each depend upon Claim 120, either directly or through other
19 dependent claims. As previously described, Claim 120 specifies a method of using a predetermined
20 arrangement of diffusion-weighted gradients to produce a plurality of outputs. The outputs are
21 vector processed to generate data representative of the anisotropic diffusion exhibited by a selected
22 structure, regardless of the alignment of the diffusion-weighted gradients with respect to the selected
23 structure. The data representative of the anisotropic diffusion are processed to generate a data set
24 that describes the shape and position of the selected structure.

25 ///

1 Not only do Hajnal et al., Suzuki et al., and Bydder et al. not teach or suggest the use of
2 vector processing in combination with diffusion-weighted gradients, these references do not teach or
3 suggest the further limitations specified in dependent Claims 130, 131, 133, and 134.

4 Claim 130, which depends upon Claim 125, specifies further limitations similar to those
5 specified by dependent Claim 123, which as discussed above specifies patentable subject matter. In
6 particular, Claim 130 specifies that the data representative of the anisotropic diffusion of curved
7 neural tissue are used to determine how to combine data sets describing different cross-sections of the
8 curved neural tissue. By combining the data sets in this manner, a description of the three-
9 dimensional shape and position of the curved neural tissue is generated. Claim 131, which depends
10 upon Claim 130, further specifies that the effective direction of the anisotropic diffusion is used when
11 determining how to combine the data sets describing the various cross-sections of the neural tissue.
12 Claim 133, which depends upon Claim 120, specifies inventive features similar to those specified in
13 Claim 130. Claim 134, which depends upon Claim 120, specifies that the predetermined arrangement
14 of gradients includes three orthogonal gradients and the corresponding outputs are processed to
15 produce an effective vector representative of the anisotropic diffusion exhibited by the selected
16 structure.

17 Rejections over Hajnal et al., Inoue, and Dixon

18 Independent Claims 92, 95, and 122 were rejected as being obvious in view of Hajnal et al.,
19 Inoue, and Dixon. Remarks accompanying these rejections state that Inoue and Dixon teach methods
20 for separating water and fat, in part by calculating the difference between water and fat signals.
21 Further remarks state that it would have been obvious to include means for calculating the difference
22 between the fat and water signals in the device of Hajnal et al. Applicants must respectfully disagree
23 with these rejections.

24 Claim 92 specifies producing a first output by applying a first diffusion-weighted gradient
25 substantially parallel to a nerve, and producing a second output by applying a second diffusion-

1 weighted gradient substantially perpendicular to the nerve. Claim 92 then specifies that the two
2 outputs are subtracted from one another to produce a data set that describes the shape and position of
3 the nerve. Inoue and Dixon do not teach the use of perpendicular and parallel diffusion-weighted
4 gradients, followed by subtracting two images generated by these gradients. Rather, both Dixon and
5 Inoue teach the use of a chemical shift fat suppression technique.⁴ These techniques are based upon
6 the fact that the magnetization frequency of water protons differs from that of fat protons.⁵ In sharp
7 contrast, the use of parallel and perpendicular diffusion-weighted gradients is based upon the principle
8 that nerves contain anisotropically diffusing water, whereas other structures do not. Furthermore, the
9 techniques taught by Dixon and Inoue are merely used to separate water from fat; the techniques are
10 not used to describe the position and shape of nerves.

11 Claim 95, which depends upon Claim 92, further specifies that the region is exposed to
12 electromagnetic fields that suppress fat prior to exposing the region to the diffusion-weighted
13 gradients. Dixon and Inoue do not in any way suggest combining fat suppression with diffusion-
14 weighted imaging as specified in Claim 95. As previously explained with respect to independent
15 Claim 135, the present inventors discovered that combining fat suppression with diffusion-weighted
16 imaging is beneficial because fat suppression increases the responsiveness of anisotropic tissue to
17 diffusion-weighted gradients.

18 Claim 122, which depends upon independent Claim 120 through dependent Claim 121,
19 specifies that the data representative of anisotropic diffusion (generated by using diffusion-weighted
20 gradients in combination with vector processing) are used to determine the optimal orientation to
21 apply perpendicular and parallel diffusion-weighted gradients. Hajnal et al., Inoue, and Dixon in no
22 ///

23
24 ⁴See, Dixon, page 1, lines 16-18; Inoue, column 1, lines 7-9.

25 ⁵See, Dixon, page 2, column 1, lines 17-21.

1 way teach or suggest determining the optimal orientation for diffusion-weighted gradients in this
2 manner, let alone also subtracting the resulting outputs to describe the shape and position of neural
3 tissue.

4 Rejection over Hajnal et al., Suzuki et al., and Gordon Sze

5 Claim 115, which depends upon Claim 89, was rejected over Hajnal et al., Suzuki et al., and
6 Gordon Sze. In addition to the fact that Claim 115 depends upon a claim, namely, Claim 89, that
7 specifies patentable subject matter, the applicants respectfully submit that Claim 115 specifies further
8 patentable limitations. While Gordon Sze teaches the use of contrast agents for imaging the spinal
9 cord (*see*, Gordon Sze, pages 195-196), it does not teach or suggest the use of contrast agents to
10 image the peripheral nerves, the cranial nerves 3-12, or the autonomic nerves.

11 Rejection over Suzuki et al. and Gordon Sze

12 Claim 140, which depends upon independent Claim 139, specifies that the excitation and
13 output arrangement means specified in Claim 139 include a phased-array coil system. The claim was
14 rejected over Suzuki et al. and Gordon Sze; remarks accompanying the rejection state that Suzuki et
15 al. teaches everything in Claim 140 except for the use of a phased-array coil system, and Gordon Sze
16 teaches the use of a phased-array coil system. Applicants respectfully disagree because, as explained
17 above with respect to Claim 139, Suzuki et al., Gordon Sze, and the other prior art of record do not
18 teach a magnetic resonance apparatus that can image peripheral nerves, cranial nerves 3-12 and
19 autonomic nerves with a conspicuity of at least 1.1 times that of surrounding non-neural tissue.
20 Specifically, Gordon Sze does not teach that simply adding phased-array coils to the system of Suzuki
21 et al. will produce a system that can effectively image nerves -- because simply adding phased-array
22 coils doesn't provide a system capable of this.

23 Rejections over Suzuki et al., Hajnal et al., and Sepponen

24 Claims 141-143 were rejected over Suzuki et al., Hajnal et al., and Sepponen. Remarks
25 accompanying these rejections state that various means to immobilize a patient are well-known, and

1 Sepponen teaches the use of markers on a frame. Applicants respectfully submit that Suzuki et al.,
2 Hajnal et al., and Sepponen do not teach or suggest a magnetic resonance apparatus as specified by
3 Claims 141-143. These claims depend upon independent apparatus Claim 139. As already explained,
4 the prior art of record does not teach an apparatus, as specified by Claim 132, that can image
5 peripheral nerves, cranial nerves 3-12, and autonomic nerves with a conspicuity that is at least 1.1
6 times that of surrounding non-neural tissue. The cited references also do not teach how to use a
7 splint to effectively image nerves; the references can't teach this, because simply using a splint does
8 not produce an apparatus with this capability. Furthermore, the references do not teach a splint that
9 is constructed to reduce edge effects, as specified by dependent Claim 143.

10 Demonstrative Video Tape

11 A video tape of nine minutes duration accompanies this response. The video tape illustrated
12 actual imaging conducted in accordance with the invention, with co-inventor Dr. Aaron G. Filler,
13 M.D., Ph.D., providing narration. Although the video tape does not include sequences in which the
14 invention is specifically compared with prior art, the applicants submit that the video tape vividly
15 demonstrates claimed features of the invention. As Dr. Fuller points out in his narration, the high
16 conspicuity set forth in Claim 89, (at least 1.1 times that of surrounding non-neural tissue) is easily
17 seen as well as the enhancement that is provided by the long T₂ sequence (spin-spin relaxation
18 coefficient) defined by dependent Claim 103. Dr. Filler also makes specific references to dependent
19 Claims 99 and 101, which specify the processing step of analyzing the output for information
20 representative of fascicles.

21 The undersigned attorneys did not directly participate in the making of the enclosed video tape
22 or suggest the narration provided by Dr. Filler. Dr. Filler, who currently is continuing his research
23 and development work in Great Britain, is familiar with both the claims of this application and the
24 prior art. The undersigned attorney has received confirmation from Dr. Filler that Dr. Filler believes
25 ///

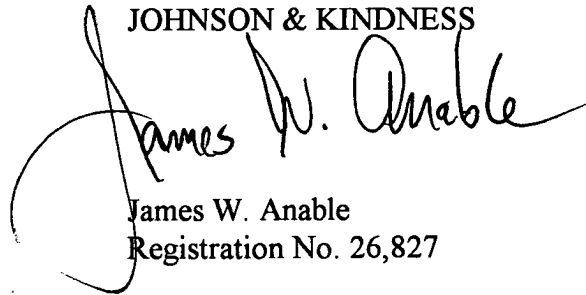
1 that the images shown in the enclosed video tape were generated in accordance with the invention as
2 it is defined by the pending claims.

3 Conclusion

4 Applicants respectfully submit that the claims present patentable subject matter and are now in
5 condition for allowance. Accordingly, applicants respectfully request the withdrawal of the claim
6 rejections, allowance of the claims, and passage of the case to early issuance. If the Examiner has any
7 questions, he is urged to call James Anable of applicants' firm of record at (206) 224-0704.

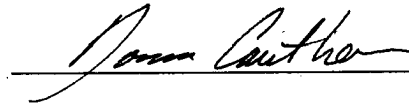
8 Respectfully submitted,

9 CHRISTENSEN, O'CONNOR,
10 JOHNSON & KINDNESS

11 
12
13 James W. Anable
14 Registration No. 26,827

15 I hereby certify that this correspondence is being deposited with the U.S. Postal Service in a
16 sealed envelope as first class mail with postage thereon fully prepaid addressed to: Commissioner of
17 Patents and Trademarks, Washington, D.C. 20231, on 11/14/94.

18 Date: 11/14/94


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20 SJP:kdr/kh/mhk
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BOX
NON-FEE
AMENDMENT



THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: A.G. Filler et al. Attorney Docket No: WRUW16938

Serial No: 08/028,795 Group Art Unit: 3305

Filed: March 8, 1993 Examiner: B. Casler

Title: IMAGE NEUROGRAPHY AND DIFFUSION ANISOTROPY IMAGING

AB

AMENDMENT TRANSMITTAL LETTER

Seattle, Washington 98101

November 14, 1994

TO THE COMMISSIONER OF PATENTS AND TRADEMARKS:

A. Amendment Transmittal

Transmitted herewith is an amendment and video tape referenced therein in the above-identified application.

X 1. No additional claim fee is required as shown below.

RECEIVED
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GROUP 330

COMPUTATION OF FEE FOR CLAIMS AS AMENDED

	Claims Remaining After Amendment		Highest Number Previously Paid For		Present Extra		Rate	Additional Fee	
Total Claims	73	Minus	81	=	0	x	\$11	=	0.00
Independent Claims	6	Minus	7	=	0	x	\$38	=	0.00

Total additional Fee for this Amendment \$0.00

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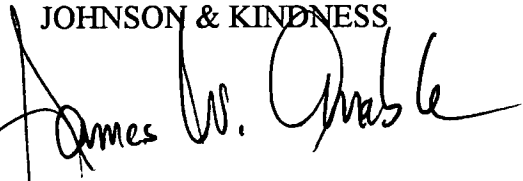
1 B. Additional Fee Charges or Credit for Overpayment

2 Please charge any additional fees or credit any overpayment to Deposit Account No. 03-1740.

3 A copy of this letter is enclosed.

4 Respectfully submitted,

5 CHRISTENSEN, O'CONNOR,
6 JOHNSON & KINDNESS

7 
8 James W. Anable
9 Registration No. 26,827
10 Direct Dial (206) 224-0704

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12 sealed envelope as first class mail with postage thereon fully prepaid addressed to: Commissioner of
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14 Date: 11/14/94

15 JWA:dc